UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,308	03/30/2004	Luca Battistini	GRT/4865-38	1799

23117 7590 04/04/2008
NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
04/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/812,308	BATTISTINI ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 10/06/07, have been fully considered but they are not deemed to be persuasive with respect to the issue of patentability. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Applicant's Appeal Brief, received 2/6/08, is acknowledged.

Upon reconsideration of applicant's arguments made of record in the amendment, filed 10/6/07, and in view of the arguments set forth in the Appeal Brief, applicant's argument are found to be persuasive to overcome the rejections made of record in the Final Office action, mailed 6/6/07. In view of the newly applied rejection(s) summarized below, the finality of the Office action, mailed 6/6/07, is hereby withdrawn. The withdrawal of the finality of said Office action renders the Appeal Brief moot.

Status of the Claims

Claims 9-11 are currently pending in this application.

Response to applicant's arguments/remarks

Applicant's arguments are rendered moot by the new bases of the rejections.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-11 are rejected under 103(a) as being unpatentable over Mistrello et al. (already made of record by applicant) and Hashimoto et al. (GB 2246350A) or Mistrello et al and Lenardo (WO 94/28926).

Mistrello et al. each DL111-IT is an immunosuppressive agent effective in inhibiting the antibody response to both thymus-dependent (SRBC) and thymus-independent (LPS) antigen (page 168, see discussion section, especially col. 1, first full

para). Instant claim 9 recites the identical compound as taught by Mistrello et al. Mistrello et al. exemplify a method of treatment comprising administering DLIII-IT in a dose of 5 mg/kg via injection to adjuvant arthritic rats, which resulted in a marked reduction of foot pad swelling (pages 164 to 166, especially page 166, section entitled "Effect on DTH"). Claim 10 recites "wherein said subject is a mammal," which overlaps with the teaching of Mistrello et al. (see pages 164 to 166). Mistrello et al. teach that the majority of immunosuppressant drugs in medicine were originally developed for treating cancer and only later were found to be useful as immunosuppresants; there is therefore a need for more selective immunosuppressants with less toxic profiles (page 163, introduction section, especially col. 1). Although Mistrello et al. is silent regarding treating humans, someone of skill in the art could reasonable envisage the use of DLIII-IT in a human subject based on the teaching of Mistrello et al. for the need to develop more selective and less toxic immunosupressant drugs. Instant claim 11 recites "wherein said subject is a human." Mistrello et al. do not teach a method of treating uveitis as claimed in the instant application.

Hashimoto et al. (GB 2246350A) teach methods of treatment comprising certain tricyclic macrolide compounds that possess immunosuppressive properties for treating autoimmune diseases, including rheumatoid arthritis and uveitis (page 8, lines 22-34).

Lenardo (WO 94/28926) teach methods of treating autoimmune diseases such as uveitis and arthritis in animals and humans (see abstract and page 5, last para.)

Based on the need to develop selective and less toxic immunosuppressants, someone of skill in the art would have been motivated to combine the teachings of Mistrello et al. with either Hashimoto et al. or Leonardo to create the instant claimed inventive concept.

Thus, someone of skill in the art at the time the instant invention was made would have deemed it obvious to create the instant invention with reasonable predictability.

Claims 9-11 are also rejected under 103(a) as being unpatentable over Rossi (WO 98/55463) and Hashimoto et al. (GB 2246350A) or Rossi and Lenardo (WO 94/28926), in further view of Kawahito et al. (Kawahito et al. Localization of quantitative trait loci regulating adjuvant induced arthritis in rats: evidence of genetic factors common to multiple autoimmune diseases. The Journal of Immunology. 1998; 161:4411-4419, electronic pages 1-19; already made of record).

Rossi teaches that DL III-IT has been proposed as an anti-gestative agent for human use, the identical compound recited in claim 9 (page 3, lines 15-19). The term "wherein said subject is a mammal" as recited in claim 10 and the term "wherein said subject is a human" as recited in claim 11, are construed to be satisfied by the teaching of Rossi (page 3, lines 15-19). Rossi teaches that triazole compounds, including DL III-IT, as being highly effective in reducing both humoural and cellular immunological response in animal models predictive for the pharmacological activity in human (page

14, lines 18-21, and page 23, line 14 to page 28, line 23). However, Rossi does not teach uveitis.

Hashimoto et al. (GB 2246350A) teach methods of treatment comprising certain tricyclic macrolide compounds that possess immunosuppressive properties for treating autoimmune diseases, including rheumatoid arthritis and uveitis (page 8, lines 22-34).

Lenardo (WO 94/28926) teach methods of treating autoimmune diseases such as uveitis and arthritis in animals and humans (see abstract and page 5, last para.)

Kawahito et al. teach that rat models appear to provide a powerful complementary approach to identify and characterize candidate genes that may contribute to autoimmune diseases in several species (abstract). Kawahito et al. teach that adjuvant-induced arthritis (AIA) in rats is a widely used autoimmune experimental model with many features similar to rheumatoid arthritis (RA) (abstract). Kawahito et al. also disclose study data of collagen-induced arthritis (CIA). Kawahito et al. teach that AIA predominantly involves T cell-mediated mechanisms, whereas CIA requires both humoral and cellular immunity (page 2, last paragraph, last line to page 3, line 1). Kawahito et al. teach that the quantitative trait loci (QTL) region on chromosome 4. *(Aia3/Cia3),* like the MHC, appears to be involved in several other autoimmune diseases in rats, including insulin-dependent diabetes, thyroiditis, and experimental autoimmune uveitis (abstract). Claim 9 recites the term "uveitis."

Based on the teaching that rheumatoid arthritis and uveitis share immunologic features coupled with the autoimmune experimental model exemplified by Kawahito et

al., someone of skill in the art would have been motivated to combine the teachings of the above cited references to create the instant claimed inventive concept in order to create a highly effective immunosuppresant agent with low toxicity.

Thus, someone of skill in the art at the time the instant invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

24 March 2008
/C. R./
Examiner, Art Unit 1611

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614